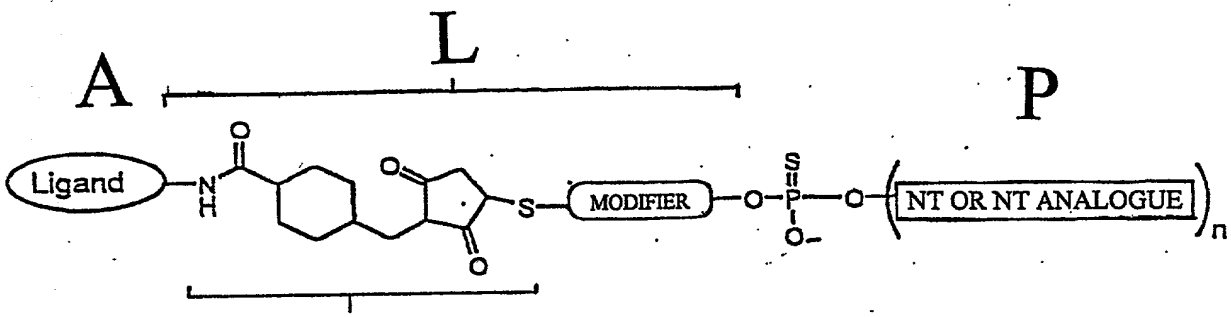
FIGURE 1



CROSS-LINKING REAGENT

FIGURE 2

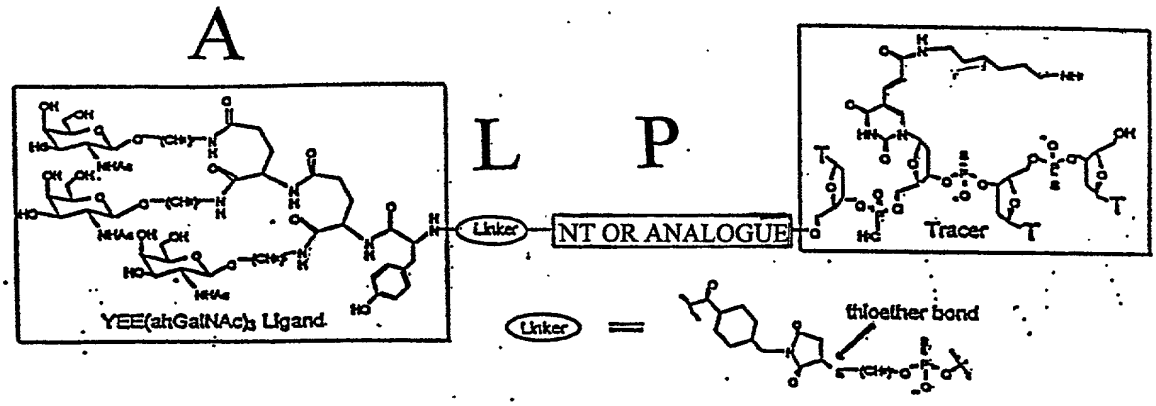
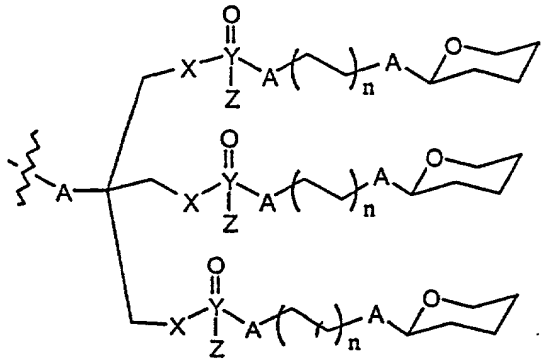
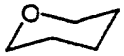


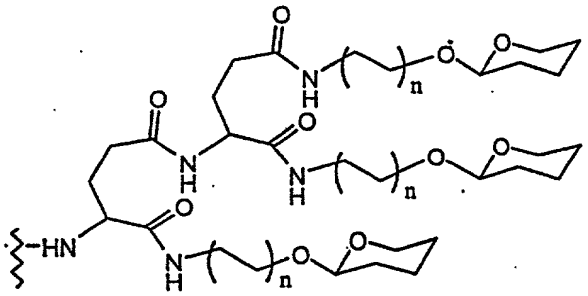
FIGURE 3

Tri-antennary

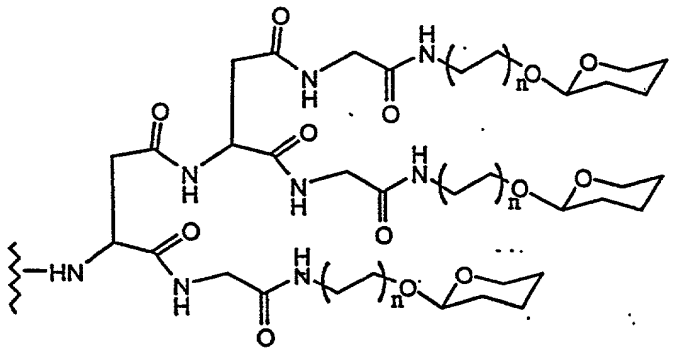


X = NH, O, S
Y = P or S
Z = NH-alkyl, NH_2, O^-, S^-
A = NH, CH_2, O, S
n = 2 to 17 2-carbon units
Carbohydrate = 

tris((heteroatom)methyl)-[heteroatom]methane



diglutamyl



diasparatyl

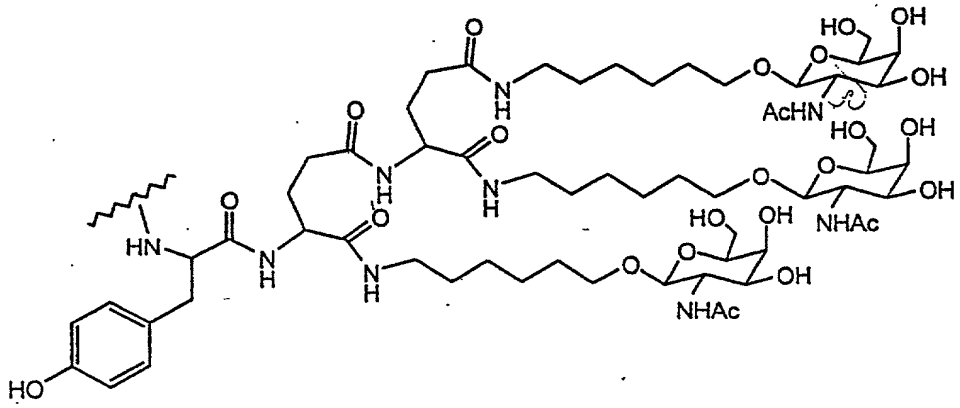
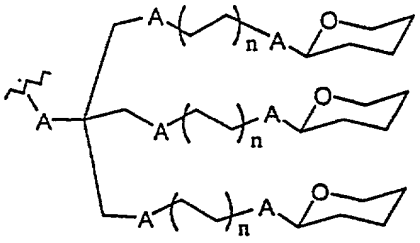
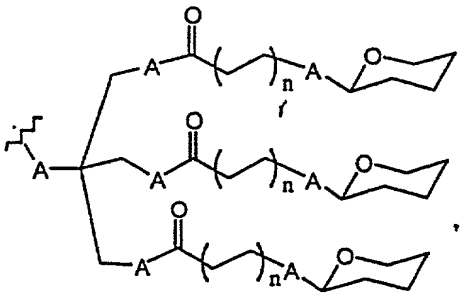


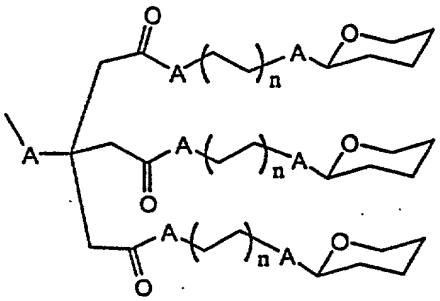
FIGURE 3 (CONTINUED)



tris((heteroatom)methyl)-[heteroatom]methane
examples
tris(hydroxymethyl)aminomethane-based
[A= O]
tris(aminomethyl)aminomethane-based
[A= NH]
tris(thiomethyl)aminomethane-based
[A= S]

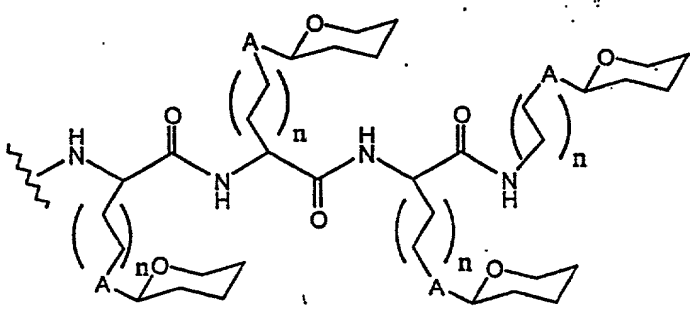


tris(aminomethyl)-[heteroatom]methane



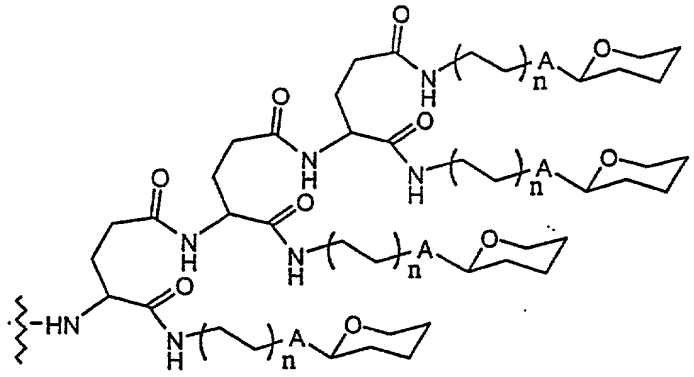
tris(acetoxy)-[heteroatom]methane

Tetra-antennary



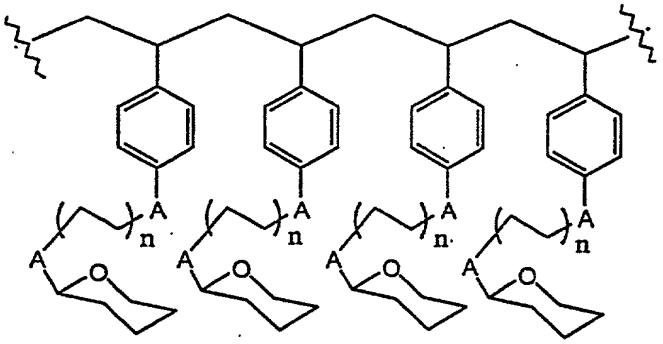
oligo(lysine)

FIGURE 3 (CONTINUED)

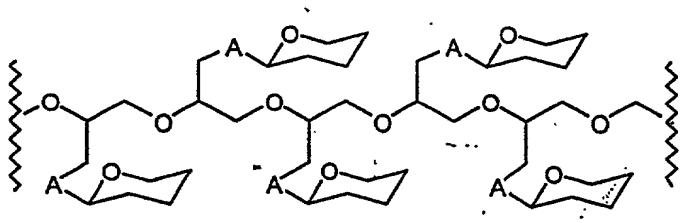


oligopeptide-based
(i.e. triglutamyl)

Multi-antennary



substituted
polystyrene-based



substituted
poly(ethyleneglycol)

FIGURE 4

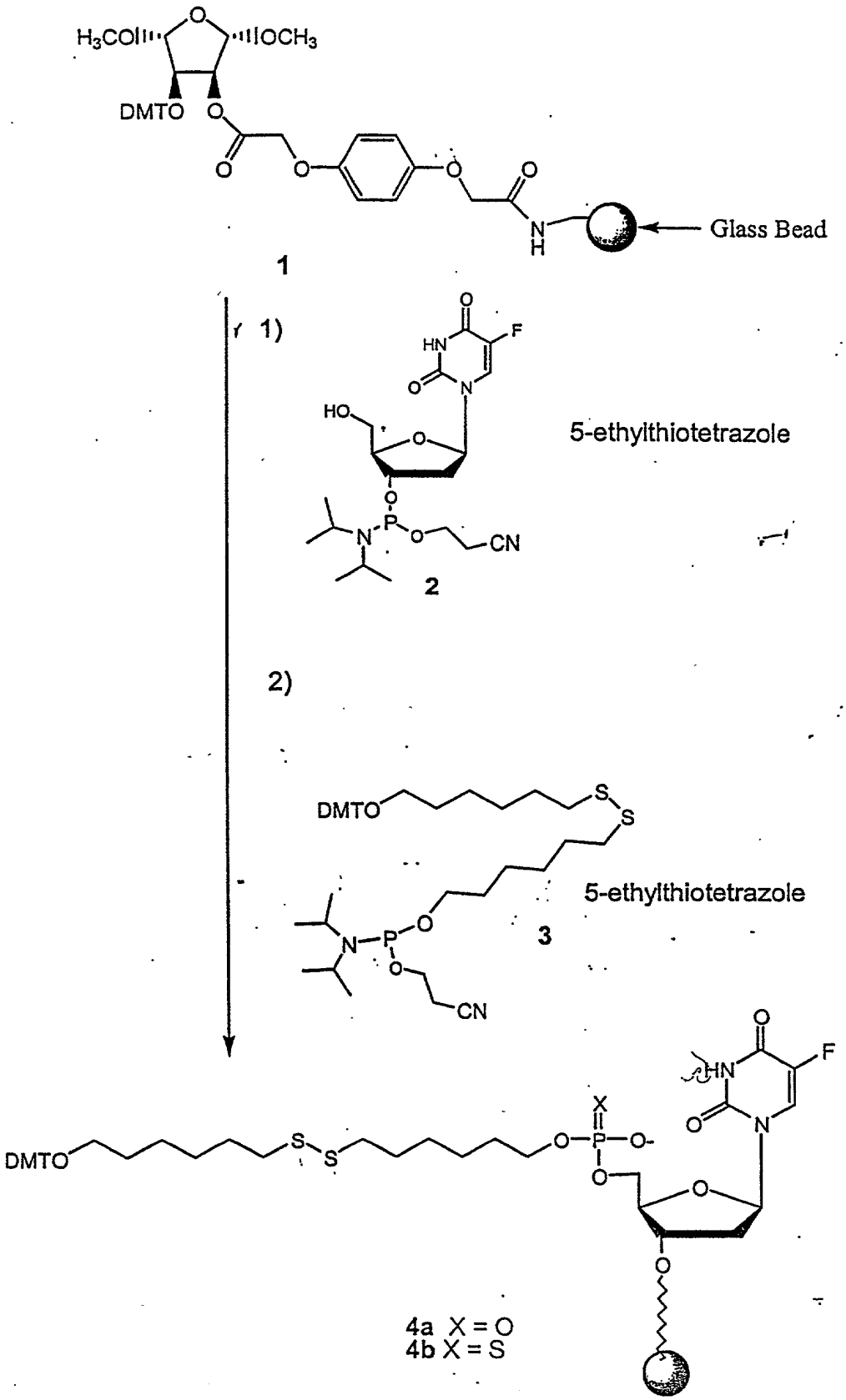
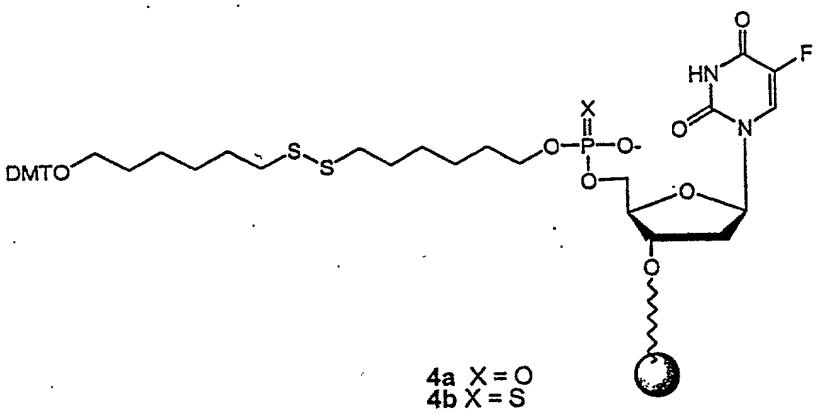

H3CO
OCH3
DMTO
O
Glass Bead
1
1)
HN
F
HO
5-ethylthiotetrazole
CN
2
2)
DMTO
S
5-ethylthiotetrazole
3
CN
DMTO
X
4a X = O
4b X = S

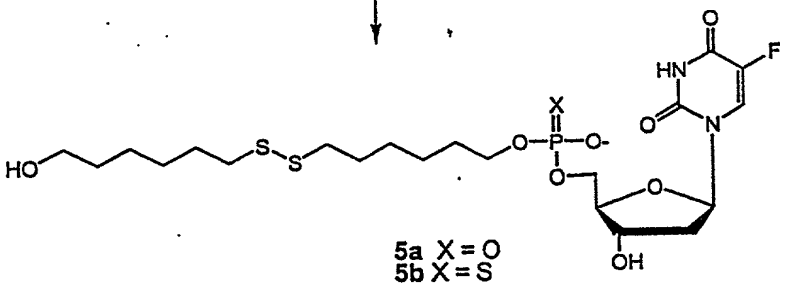
FIGURE 5



4a X = O
4b X = S

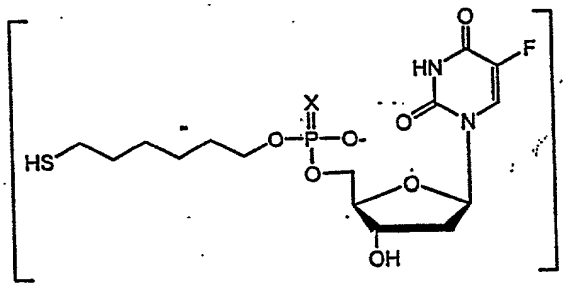
f

C18 SepPak™
1% CF_3COOH



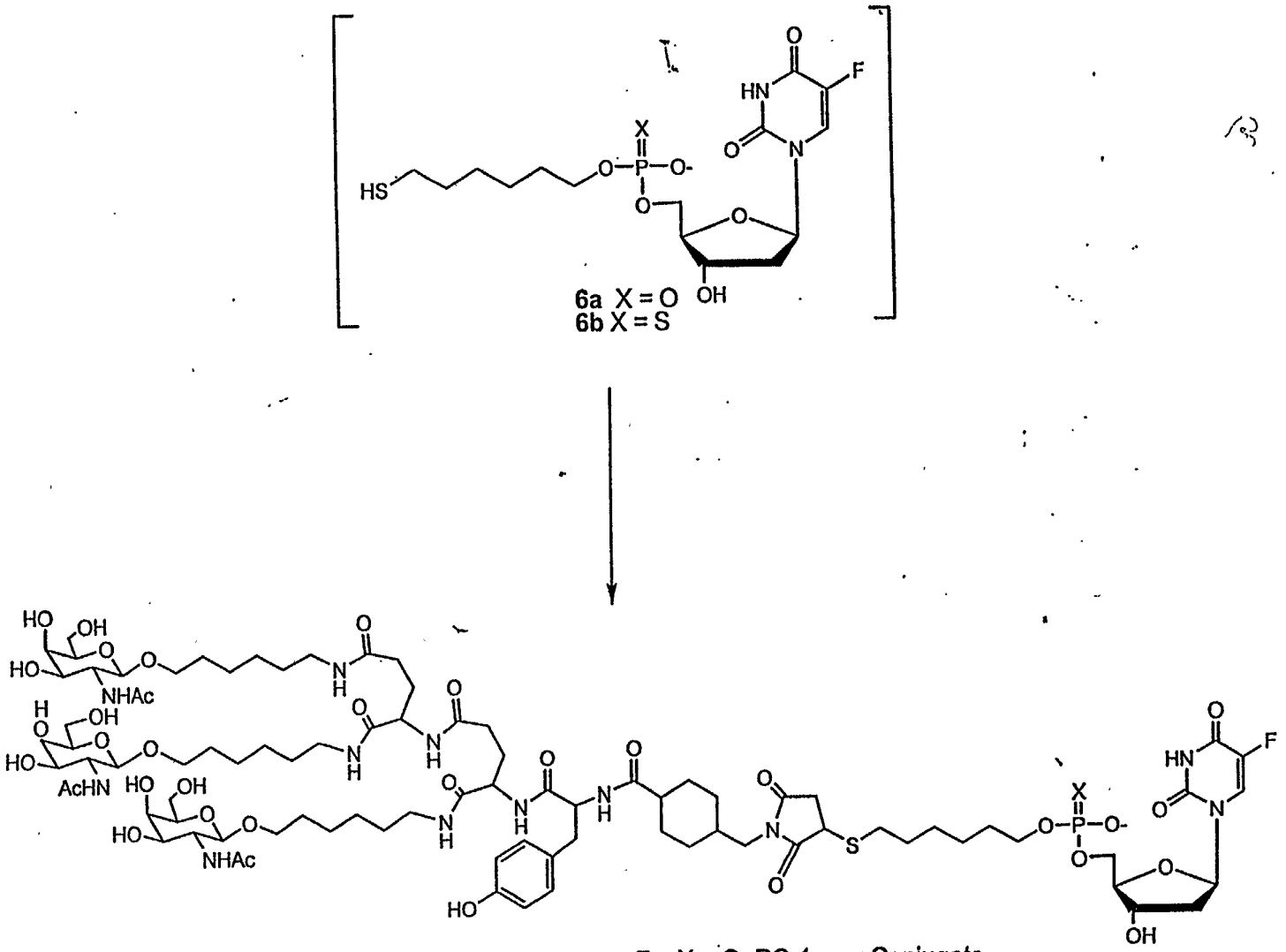
5a X = O
5b X = S

DTT



6a X = O
6b X = S

FIGURE 6



7a X = O; PO 1-mer Conjugate
7b X = S; PS 1-mer Conjugate

FIGURE 7

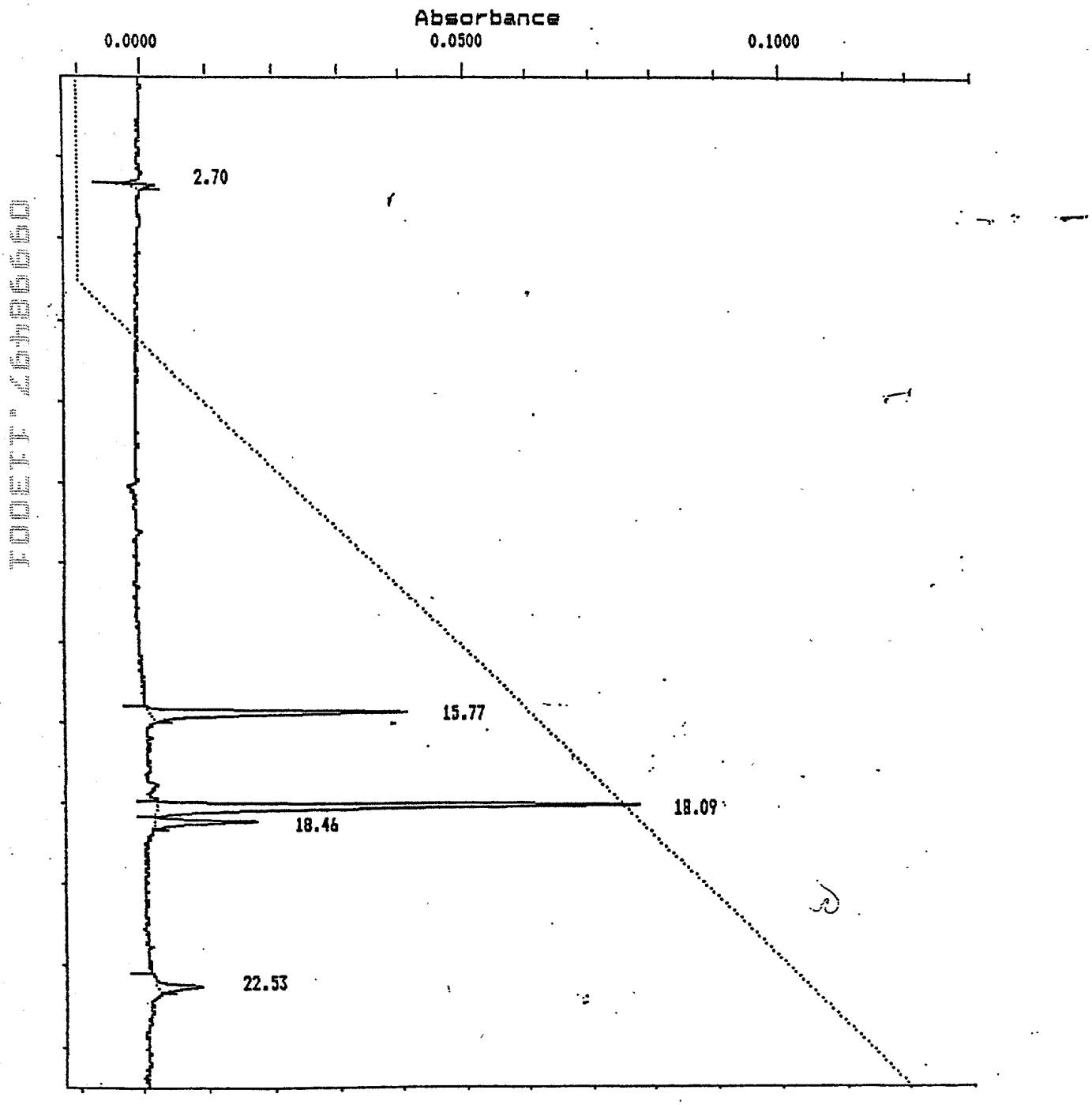


FIGURE 8

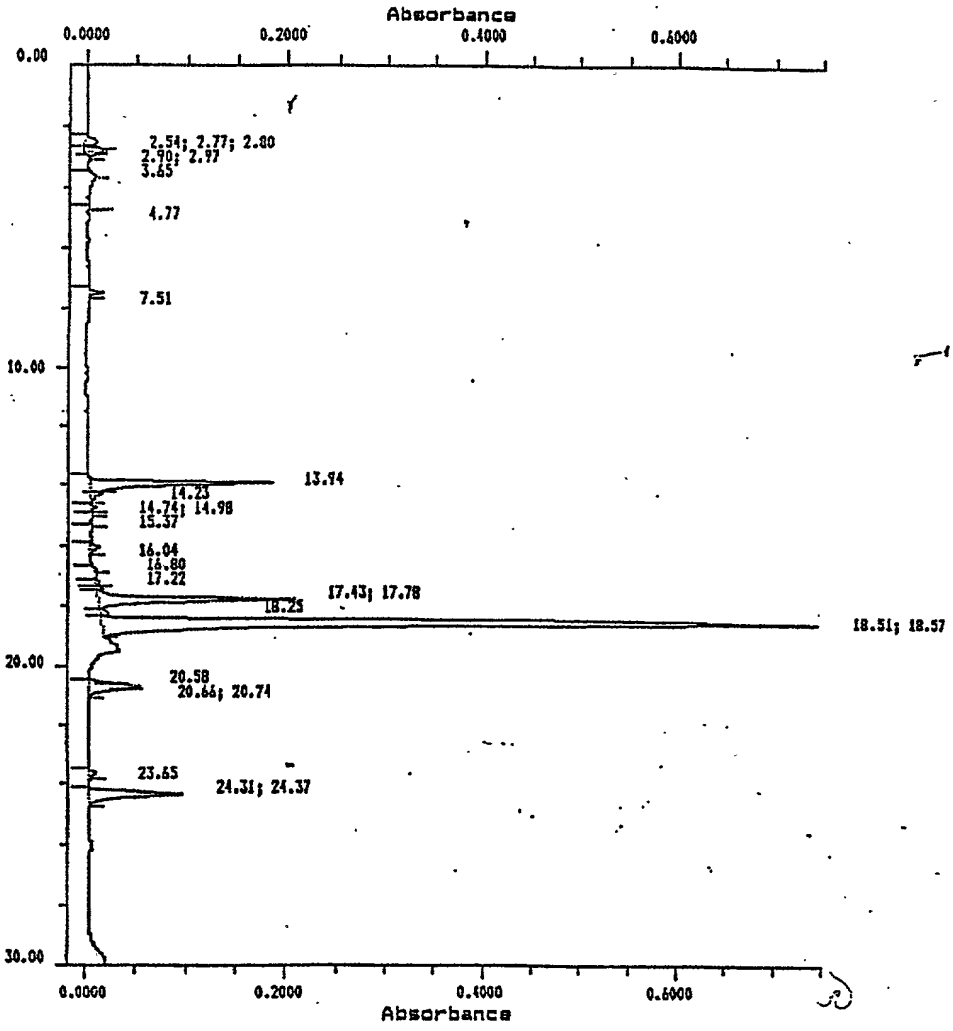

Absorbance
0.0000
0.2000
0.4000
0.6000
0.00
10.00
20.00
30.00
2.54; 2.77; 2.80
2.90; 2.97
3.65
4.77
7.51
13.94
14.23
14.74; 14.98
15.37
16.04
16.60
17.22
17.43; 17.78
18.25
18.51; 18.57
20.58
20.66; 20.74
23.65
24.31; 24.37
Absorbance

FIGURE 9

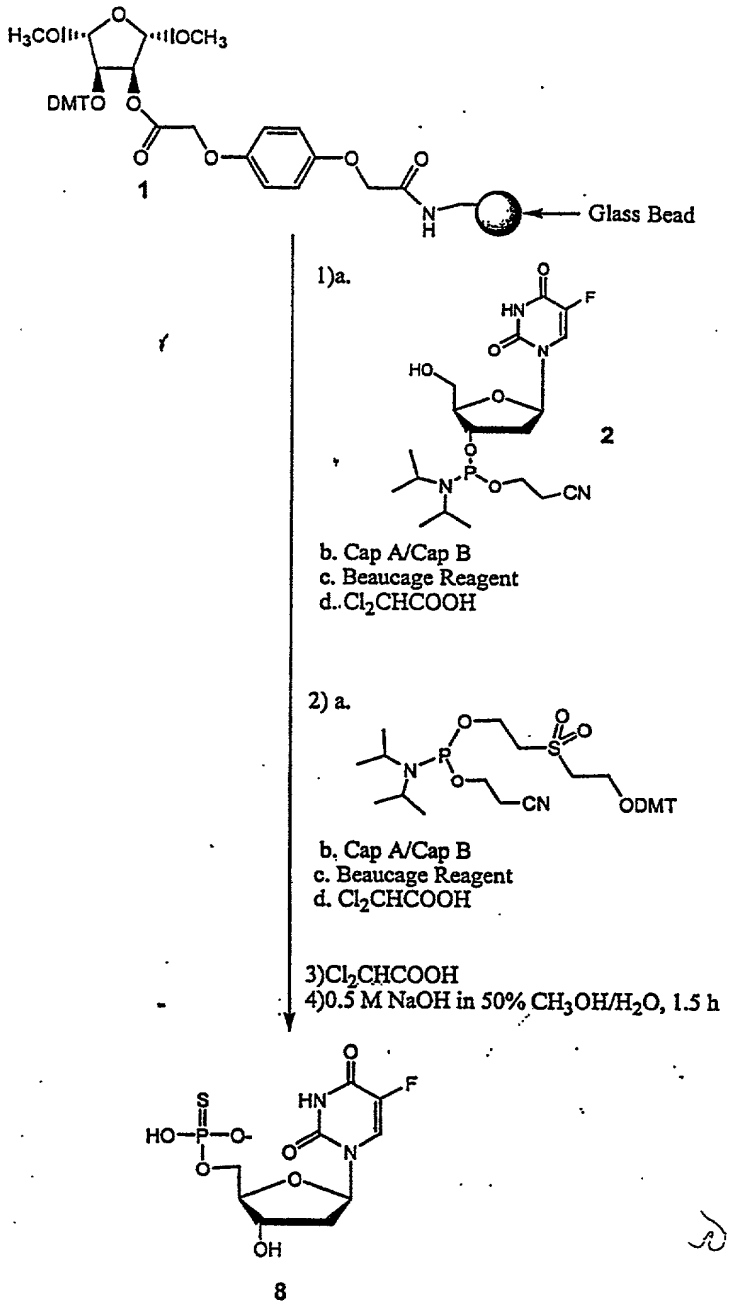

H3CO
OCH3
DMTO
O
1
Glass Bead
1)a.
HO
F
HN
2
CN
b. Cap A/Cap B
c. Beaucage Reagent
d. Cl2CHCOOH
2) a.
CN
ODMT
b. Cap A/Cap B
c. Beaucage Reagent
d. Cl2CHCOOH
3)Cl2CHCOOH
4)0.5 M NaOH in 50% CH3OH/H2O, 1.5 h
HO
OH
8

FIGURE 10

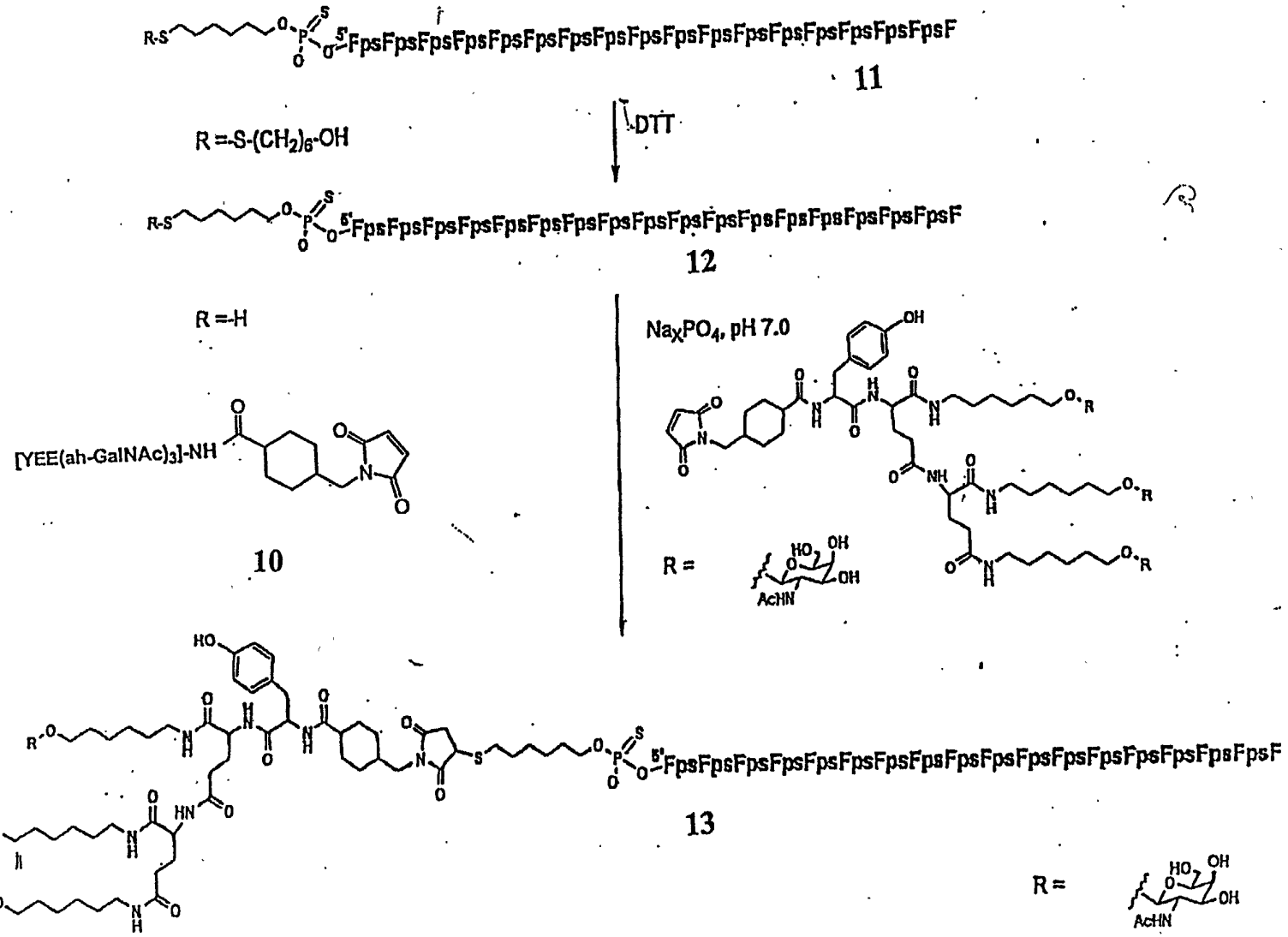
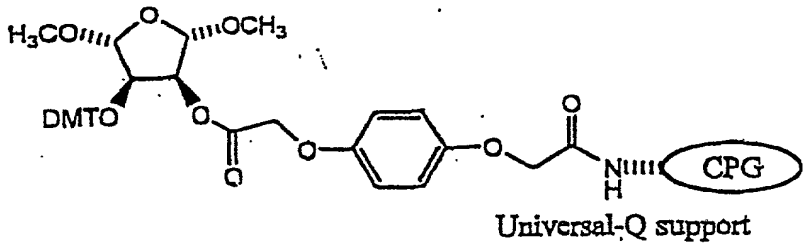

R-S
5'FpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsF
11
R =-S-(CH2)6-OH
DTT
12
R =-H
NaXPO4, pH 7.0
[YEE(ah-GalNAc)3]-NH
10
R =
AcHN
13

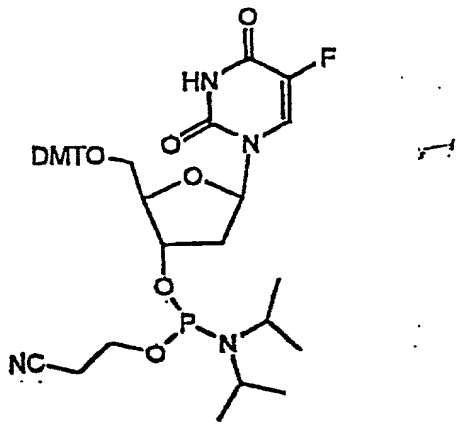
FIGURE 11



Universal-Q support

1) H+

2) 1H-tetrazole

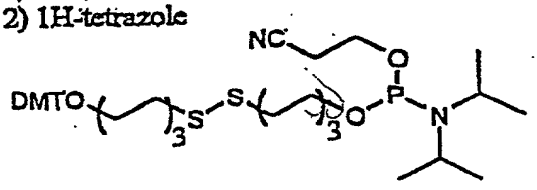


3) Oxidation - Beaucage Reagent
4) Capping - Acetic anhydride, 2,6-Lutidine
Tetrahydrofuran

5) Repeat

DMTO-FpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsF-Q

1) H+
2) 1H-tetrazole

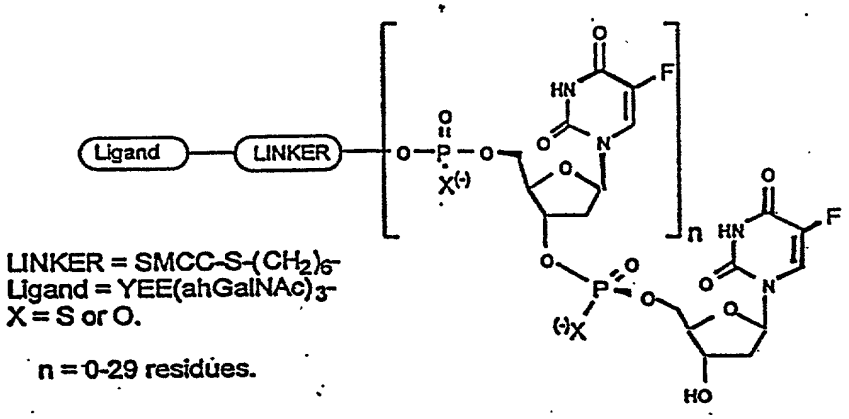


3) Oxidation - Beaucage Reagent
4) Capping - Acetic anhydride, 2,6-Lutidine
Tetrahydrofuran

5) H+
6) 0.1 M NaOH in 50% CH_3OH/H_2O, 1h, 25°C
7) C_{18} SepPak (Waters Corp.)

HO-$(CH_2)_6$-SS-$(CH_2)_6$-ps-FpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsFpsF

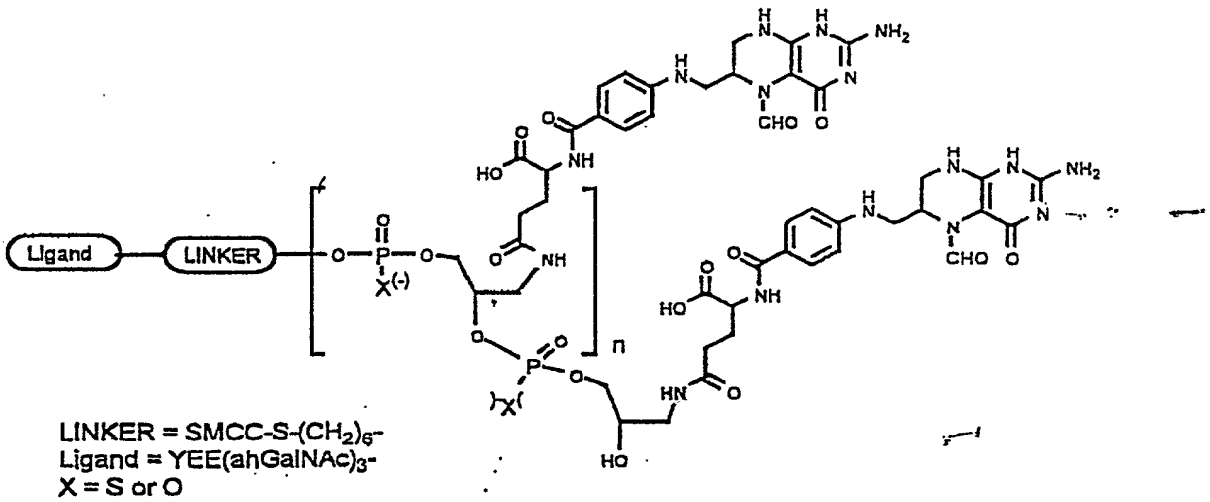
FIGURE 12



LINKER = SMCC-S-$(CH_2)_6$-
Ligand = YEE(ahGalNAc)$_3$-
X = S or O.

n = 0-29 residues.

FIGURE 13



LINKER = SMCC-S-$(CH_2)_6$-
Ligand = YEE(ahGalNAc)$_3$-
X = S or O
n = 0-19 residues.